Office Action Summary	Application No. 08/750,101	Applicant(s) DOLLY ET AL
	Examiner N. M. Minnifield	Group Art Unit 1645

☒ Responsive to communication(s) filed on *Jul 30, 1998*.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-4, 7, 8, and 22-25* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-4, 7, 8, and 22-25* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☒ The proposed drawing correction, filed on *Apr 3, 1998* is ☒approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *13*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Response to Amendment

Sequence Requirements

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). A computer readable form (CRF) of the sequence listing was submitted on April 3, 1998. However, the CRF could not be processed by the Scientific and Technical Information Center (STIC) for the reason(s) set forth on the attached CRF Diskette Problem Report. Direct the reply to the undersigned. Applicant is requested to return a copy of the attached CRF Diskette Problem Report with the reply.

2. Full compliance with the sequence rules is required in response to this office action. A complete response to this office action should include both compliance with the sequence rules and a response to the Office Action set forth below. Failure to fully comply with ***both*** these requirements in the time period set forth in this office action will be held non-responsive.

3. Applicants' amendment filed July 30, 1998 is acknowledged and has been entered. Claim 4 has been amended. Claims 15-21 and 26-32 have been canceled. Claims 1-4, 7, 8 and 22-25

are now pending in the present application. All prior art rejections have been withdrawn, in view of Applicants' amendment, with the exception of those discussed below.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. The corrected or substitute drawings were received on May 15, 1998. These formal drawings have been reviewed and approved by the Draftsman. However, the figure descriptions for figures 1 and 6 in the specification are not the same as the formal drawings. The formal drawings have figure 1A and 1B or figure 6A and 6B, but the figure descriptions in the specification only refer to figure 1 or figure 6. Correction is required prior to issuance of the application to avoid any printer queries and/or delays in the publication of the patent.

6. Applicant's election with traverse of Group I, claims 1-4, 7, 8 and 22-25, in Paper No. 12 is acknowledged. The traversal is on the ground(s) that the Examiner must examine all pending claims, even if distinctness or independence is shown, unless a serious burden would result from such examination. Applicants further assert that there is no indication that the two restriction groups represent inventions that have acquired a separate status in the art; nor is there any evidence that the subjects of the two groups of claims have attained recognition in the art as subjects for inventive effort, thus resulting in separate classification. Applicants have asserted

that claim 15 is a linking claim being generic to the species that the Examiner has indicated exist and that claim 15 should be examined with Group I and if this Group I is found patentable, the claims of Group II should be examined as well. This is not found persuasive because the restriction is set forth according to practice set forth under 35 USC 121 and 372 (PCT rule 13.1). Applicants are entitled to a product, method of making the product and method of using said product, which is set forth in Group I. The inventions of Group I and Group II are distinct in that they have different functions, and different biochemical characteristics. It is noted that there was no species requirement set forth.

The requirement is still deemed proper and is therefore made FINAL.

7. Claims 1, 2, 7 and 8 are rejected under 35 U.S.C. 102(b) as anticipated by Bizzini.

Bizzini discloses a composition that comprises tetanus toxin and is bound to a thiol group, and that this composition can be used to transport agents for medicine to the central nervous system (abstract; col. 2, l. 56-60). Bizzini discloses the use of fragments of the tetanus toxin that are atoxic (i.e. inactive) (col. 2, l. 36-45). Bizzini discloses that medicines can be transported into the nervous system via the medicine being bound to the thioliated polypeptide compound (tetanus toxin), employed as a transport agent (col. 6, l. 1-40; claims).

The prior art anticipates the claimed invention.

The rejection is maintained for the reasons of record. Applicant's arguments filed July 30, 1998 have been fully considered but they are not persuasive. Applicants have asserted that Bizzini et al is limited to a single Clostridial neurotoxin: tetanus toxin, and that Bizzini et al recites the property of retrograde axonal transport, which is not a property of other Clostridial toxins such as botulinum toxin. However, the claims are directed to an inactive Clostridial toxin (claims 1, 7 and 8) and claim 2 sets forth that the Clostridial neurotoxin can be tetanus toxin which is disclosed in the prior art. With regard to the properties, it is noted that applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., retrograde axonal transport) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore the prior art anticipates the claimed invention.

8. Claims 1, 2, 7 and 24 are rejected under 35 U.S.C. 102(e) as anticipated by Mond et al.

Mond et al disclose a construct comprising two immunogenic carriers, and that such constructs are suitable for use in the diagnosis, treatment, and prevention of diseases (abstract). The prior art discloses a tetanus toxin coupled (i.e. attached) to a bioactive molecule (*H. influenzae* PRP) (col. 16-17). The prior art discloses the use of tetanus toxoid, therefore it is inactive (claims).

The prior art anticipates the claimed invention.

The rejection is maintained for the reasons of record. Applicant's arguments filed July 30, 1998 have been fully considered but they are not persuasive. Applicants have asserted that the prior art does note disclose internalization and that the whole idea of the conjugate of Mond is to recruit T cells in the extracellular environment. Applicants have asserted that there is only a disclosure of tetanus toxins, not a variety of Clostridial toxins. However, the claims are directed to an inactive Clostridial toxin (claims 1, 7 and 8) and claim 2 sets forth that the Clostridial neurotoxin can be tetanus toxin which is disclosed in the prior art. The prior art discloses the claimed invention. With regard to the properties, it is noted that the function of the product or composition is the same and therefor applicants claimed properties are inherent. Mond discloses that toxins are injected to protect against tetanus and botulism (col. 1, l. 28-33). Mond disclose that the composition or construct is prepared from non-toxic components (col. 5, l. 11-12). Mond discloses that the constructs can be applied to therapy, prophylaxis, diagnosis and research (col. 5, l. 18-20). Further it is noted that the limitations argued by Applicants are not set forth in the pending claims. It is noted that the since the Office does not have the facilities for examining and comparing applicants' product and methods against the product and method of the prior art, the burden is on applicant to show a novel or unobvious differences between the claimed product and methods and the product and methods of the prior art (i.e., that the product and methods of the prior art does not possess the same material structural and functional characteristics of the claimed product and methods) See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594. Therefore the prior art anticipates the claimed invention.

9. Claims 1, 2, 7, 8, and 22-24 are rejected under 35 U.S.C. 102(e) as anticipated by Halpern.

Halpern discloses the tetanus toxoid conjugated to a carrier protein and that this composition is useful in methods of treating tetanus infection which has manifestations of neurological systems including muscle spasms (abstract; p. 1; p. 3; p. 8).

The prior art anticipates the claimed invention.

The rejection is maintained for the reasons of record. Applicant's arguments filed July 30, 1998 have been fully considered but they are not persuasive. Applicants have asserted that the prior art is concerned with the preparation of an immunogen against tetanus toxin and that the disclosure is limited to the use of fragment of tetanus toxin. Applicants have asserted that as with Mond internalization of an inactive toxin molecule linked to a drug is not taught; therefore every element of the rejected claims has not been found in the applied reference and cannot anticipate. The claims recite comprising which does not exclude other component (the neurotoxin could be a fragment); further with regard to the properties, it is noted that the function of the product or composition is the same and therefor applicants claimed properties are inherent. It is noted that the since the Office does not have the facilities for examining and comparing applicants' product and methods against the product and method of the prior art, the burden is on applicant to show a novel or unobvious differences between the claimed product and methods and the product and methods of the prior art (i.e., that the product and methods of the prior art does not possess the

same material structural and functional characteristics of the claimed product and methods) See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594. Therefore the prior art anticipates the claimed invention.

13. Claims 3 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bizzini taken with Fraenkel-Conrat et al.

Bizzini teaches a composition that comprises tetanus toxin and is bound to a thiol group, and that this composition can be used to transport agents for medicine to the central nervous system (abstract; col. 2, l. 56-60). Bizzini teaches the use of fragments of the tetanus toxin that are atoxic (i.e. inactive) (col. 2, l. 36-45). Bizzini teaches that medicines can be transported into the nervous system via the medicine being bound to the thioliated polypeptide compound (tetanus toxin), employed as a transport agent (col. 6, l. 1-40; claims). The prior art teaches the claimed invention except or the concept of amino acid modification of the neurotoxin. However, Fraenkel-Conrat et al teach amino acid substitution of the light chain of tetanus toxin. Fraenkel-Conrat et al also teach fusion (attachment) of another bioactive molecule. Fraenkel-Conrat et al teach that the mutant light chain of tetanus toxin was inactive. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the inactive and modified neurotoxin of Fraenkel-Conrat et al in a composition for the purpose of treating tetanus infection. Both references teach the concept of using inactive neurotoxins. The claimed

invention id prima facie obvious in view of Bizzini taken with Fraenkel-Conrat et al, absent any convincing evidence to the contrary.

The rejection is maintained for the reasons of record. Applicant's arguments filed July 30, 1998 have been fully considered but they are not persuasive. Applicants have asserted that the light chain is attenuated to make the molecule non-toxic and that thiolation of the toxin is not disclosed or claimed. Applicants have asserted that the prior art toxins do not have the same properties as the claimed invention (intraneuronal retrograde transport). Applicants have asserted that there is no suggest to combine the prior art references. It is noted that this is a combination 103 obviousness rejection over what Bizzini et al in view of Fraenkel-Conrat taken together would suggest to person having ordinary skill in the art at the time the invention was made. Bizzini suggests reducing the toxicity of the tetanus toxin therefore it would have been obvious to a person having ordinary skill in the art at the time the invention was made to modify the neurotoxin by any means (inactivation, attenuation, deletion or substitution of amino acids) which would alter the neurotoxin. The claimed invention is prima facie obvious in view of the prior art absent any convincing evidence to the contrary.

14. No claims are allowed.

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is (703) 305-3394. The examiner can normally be reached on Monday-Thursday from 7:00 AM-4:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D., can be reached on (703) 308-3995. The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

N. M. Minnifield

January 26, 1999

NITA MINNIFIELD
PRIMARY EXAMINER